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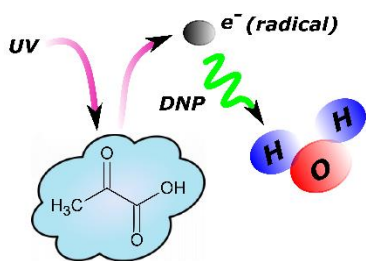
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# Preparation of Radical-Free Hyperpolarized Water using Photo-induced non-persistent Radicals on a “SpinLab-like” dissolution-DNP Polarizer

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The polarization of nuclear spins in radical-doped frozen amorphous solid samples can be enhanced by dynamic nuclear polarization (DNP) at low temperature and moderate magnetic field (usually between 3.35 T and 7 T). The polarization is maintained in a rapid dissolution procedure to obtain liquid-state hyperpolarized (HP) molecules in solution [1,2]. In the biomedical field, dissolution-DNP gained more and more success in the last decade since it represents a promising tool for early cancer diagnosis and real time metabolic studies [3,4]. Although dissolution-DNP can potentially be employed to increase the polarization of any non-zero nuclear spin species, the method has mainly been used to study biological molecules labeled with <sup>13</sup>C in a position with a long T<sub>1</sub>. The electron spins introduced in the sample, which embody the source for the polarization transfer to the nuclei in the solid state, become unwanted at the moment of dissolution and transfer of the HP liquid since they represent the main source of spin relaxation, and thus polarization loss.

A typical example is the short T<sub>1</sub> of water protons (<sup>1</sup>H) when a paramagnetic agent is present in the solution.

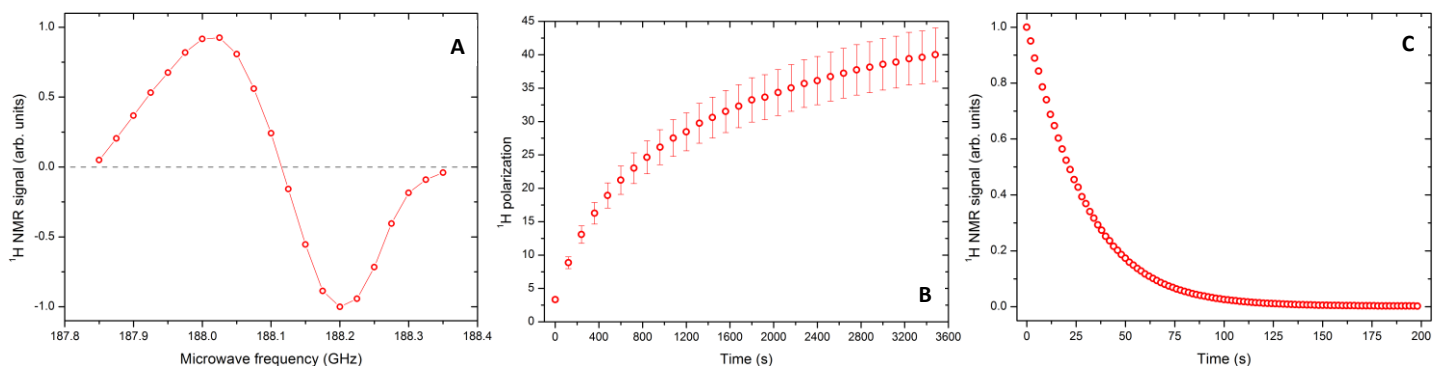
Nevertheless it has recently been demonstrated that HP water, obtained via dissolution-DNP, can be successfully employed to obtain angiographic and perfusion images with high spatial resolution [5, 6]. These pioneering studies provided a novel contrast agent, free of paramagnetic metal ions such as Gd, and based on water only. However they also clearly established the limitations of the state-of-the-art: even though a polarization of about 70% was measured at 6.7 T and 1.2 K in the solid state, after dissolution, once transferred to the measuring apparatus, only 5% of water proton polarization was left in the liquid state [6]. The main reason of this dramatic polarization's reduction has to be attributed to the time employed in scavenging the radical (the procedure takes about 10 s during which the proton T<sub>1</sub> is still 3 – 4 s) [5].

In the present study we show a novel solution to circumvent this issue by employing non-persistent radicals generated by low-temperature, UV-irradiation of pyruvic acid (PA) aqueous solutions. These radicals, in sufficiently high concentration to perform DNP at cryogenic temperature, suffer from thermal stress above 190 K [7]. Thus, they are annihilated within the dissolution procedure, when the DNP sample temperature increases, leaving a HP solutions naturally free of paramagnetic entities [8, 9].

The DNP sample choice was a compromise between good glassing properties and high radical yield after irradiation: a mixture of PA:H<sub>2</sub>O 1:1 (v/v) was used [8, 9]. 50 frozen pellets were made pouring 2.5  $\mu$ L droplets of the liquid sample into a transparent quartz dewar (Wilma-LabGlass WG-850-B-Q) filled with liquid nitrogen. The sample was irradiated for 100 s with a high power (20 W/cm<sup>2</sup>) broad-band UV source (Dymax BlueWave 75). X-band ESR measurements (Bruker EMX) showed a radical concentration of 42 $\pm$ 2 mM.

The sample was then transferred to a homebuilt 6.7 T dissolution-DNP polarizer equipped with the GE SPINlab fluid path technology for inserting the sample (see [10] for an extensive description of the system). The original sample vial was replaced by a custom-made PTFE reusable threaded vial to facilitate the loading of the temperature sensitive UV-beads.

DNP was performed at 6.7 T and 1.2 K with microwave irradiation with a nominal output power of 55 mW and at a frequency of 188.025 GHz according to the positive maximum of the <sup>1</sup>H microwave sweep (see Fig. 1A). A maximum proton polarization of 40 $\pm$ 4% was measured in the solid state (see Fig. 1B). The dissolution was performed with D<sub>2</sub>O at 130°C collecting in a syringe 2 mL of HP final solution. The latter was then injected into a 5 mm NMR tube and transferred to a Varian 400 MHz high resolution NMR spectrometer. The <sup>1</sup>H signal was acquired with 5° pulses every 2 s (see Fig 1C). A water proton T<sub>1</sub> of 30.5 $\pm$ 0.5 s was measured confirming the absence of radical in the HP solution.



**Figure 1.** Proton DNP microwave sweep at 6.7 T and 1.2 K (A). Proton DNP buildup measured shining microwaves at a frequency of 188.025 GHz and 55 mW of output power (B). Water's proton relaxation measured at room temperature in a Varian 400 MHz high resolution NMR spectrometer (C).

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